

**IN THE CLAIMS:**

The following claim listing will replace all previous listings of the claims:

1-73. (Canceled)

74. (Withdrawn) A method for producing in methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells, comprising providing a methylotrophic yeast strain, which does not express at least one enzyme involved in production of high mannose structures; and introducing into the yeast strain at least one enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub>.

75. (Withdrawn) The method of claim 74, wherein said enzyme involved in production of high mannose structures is alpha-1,6-mannosyltransferase encoded by the OCH1 gene.

76. (Withdrawn) The method of claim 74, wherein said methylotrophic yeast strain is an OCH1 mutant strain.

77. (Withdrawn) The method of claim 76, wherein said OCH1 mutant strain is made by transforming a wild type methylotrophic yeast strain with the vector of claim 47.

78. (Withdrawn) The method of claim 74, wherein said enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub> is a mannosidase or glucosidase.

79. (Withdrawn) The method of claim 78, wherein said mannosidase is  $\alpha$ -1,2-mannosidase.

80. (Withdrawn) The method of claim 78, wherein said glucosidase is glucosidase II.

81. (Withdrawn) The method of claim 74, wherein said enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub> is of a fungal origin or a mammalian origin.

82. (Withdrawn) The method of claim 74, wherein said enzyme for production of

Man<sub>5</sub>GlcNAc<sub>2</sub> is targeted to a subcellular location in said methylotrophic yeast where it is optimal to produce Man<sub>5</sub>GlcNAc<sub>2</sub>.

83. (Withdrawn) The method of claim 82, wherein said subcellular location is the ER.

84. (Withdrawn) The method of claim 74, wherein said methylotrophic yeast is of the genera *Candida*, *Hansenula*, *Torulopsis*, or *Pichia*.

85. (Withdrawn) The method of claim 84, wherein said methylotrophic yeast is selected from *Pichia pastoris*, *Pichia methanolica*, *Pichia anomola*, *Hansenula polymorpha* or *Candida boidinii*.

86. (Withdrawn) A method for producing in methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells, comprising providing a methylotrophic yeast strain, which does not express at least one enzyme involved in production of high mannose structures; and introducing into the yeast strain at least one enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub>, wherein said enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub> is targeted to a subcellular location in said methylotrophic yeast where it is optimal to produce Man<sub>5</sub>GlcNAc<sub>2</sub>.

87. (Withdrawn) A method for producing in methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells, comprising providing a methylotrophic yeast strain, which does not express at least one enzyme involved in production of high mannose structures; and introducing into the yeast strain at least one enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub>, wherein said enzyme for production of Man<sub>5</sub>GlcNAc<sub>2</sub> is targeted to a subcellular location in said methylotrophic yeast and wherein said subcellular location is the ER.

88. (Withdrawn) A method for producing in a methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells, comprising introducing into the yeast at least one enzyme for the production of Man<sub>5</sub>GlcNAc<sub>2</sub>, and producing said glycoproteins in said yeast.

89. (Withdrawn) A method for producing in methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells, comprising providing a methylotrophic yeast strain which does not express at least one enzyme involved in production of high mannose structures, and producing said glycoproteins in said strain.

90. (Currently amended) A genetically engineered strain of *Pichia*, wherein said strain is transformed with a ~~vector capable of expressing~~a nucleotide sequence coding for a *T. reesei*  $\alpha$ -1,2-mannosidase or a functional part thereof wherein said  $\alpha$ -1,2-mannosidase or said functional part is genetically engineered to contain an ER-retention signal, in said strain, wherein said vector comprises a nucleotide sequence coding for said  $\alpha$ -1,2-mannosidase or said functional part, and wherein the genomic Och1 gene in said strain is disrupted such that said strain fails to produce a functional Och1 protein, and wherein as a result of expression of said  $\alpha$ -1,2-mannosidase or said functional part, said strain produces  $\text{Man}_5\text{GlcNAc}_2$  as a predominant N-glycan structure or a predominant intermediate N-glycan structure.

91. (Canceled)

92. (Currently amended) The strain of claim ~~[[91]]~~90, wherein said ER-retention signal comprises the peptide HDEL (SEQ ID NO: 1).

93. (Previously presented) The strain of claim 90, wherein the nucleotide sequence coding for said  $\alpha$ -1,2-mannosidase or said functional part is operably linked to a promoter and a 3' termination sequence.

94. (Previously presented) The strain of claim 93, wherein said promoter is the promoter of a gene selected from the group consisting of AOXI, AOXII, GAP, and FLD.

95. (Previously presented) The strain of claim 90, wherein said strain is a *Pichia pastoris* strain.

96. (Canceled)

97. (Previously presented) The strain of claim 90, further transformed with a vector which comprises a nucleotide sequence coding for a glucosidase II or a functional part thereof.

98. (Previously presented) The strain of claim 97, wherein said glucosidase II is from a fungal species or a mammalian species.

99. (Previously presented) The strain of claim 98, wherein said fungal species is *Saccharomyces cerevisiae*.

100. (Previously presented) The strain of claim 97, wherein said glucosidase II or said functional part is tagged with an ER-retention signal.

101. (Previously presented) The strain of claim 100, wherein said ER-retention signal comprises the peptide HDEL (SEQ ID NO: 1).

102. (Previously presented) The strain of claim 97, wherein the nucleotide sequence coding for said glucosidase II or said functional part is operably linked to a promoter and a 3' termination sequence.

103. (Previously presented) The strain of claim 102, wherein said promoter is the promoter of a gene selected from the group consisting of AOXI, AOXII, GAP, and FLD.

104. (Currently amended) The strain according to any one of claims [[90-103]]90, 92-95 or 97-103, further transformed with a nucleic acid sequence coding for and capable of expressing a heterologous glycoprotein.

105. (Currently amended) A kit comprising a strain according to any one of claims [[90-97]]90, 92-95 or 97.

106. (Currently amended) A method of producing a glycoprotein with reduced

glycosylation in *Pichia*, comprising obtaining a genetically engineered strain of *Pichia* according to any one of claims [[90-103]]90, 92-95 or 97-103, and producing said glycoprotein from said strain.

107. (Currently amended) A method of reducing glycosylation of a heterologous glycoprotein expressed in a *Pichia* strain, comprising transforming cells of said strain with a nucleotide sequence coding for a *T. reesei*  $\alpha$ -1,2-mannosidase or ~~said~~ a functional part thereof wherein said  $\alpha$ -1,2-mannosidase or said functional part is genetically engineered to contain an ER-retention signal, and with a nucleotide sequence comprising a portion of the genomic OCH1 gene of said strain operably linked to a selectable marker, such that said  $\alpha$ -1,2-mannosidase or said functional part thereof is expressed in transformed cells, and the genomic OCH1 gene of said strain is disrupted, wherein said cells are also transformed with a nucleotide sequence coding for said heterologous glycoprotein; and producing said glycoprotein from the transformed cells, wherein said glycoprotein comprises Man<sub>5</sub>GlcNAc<sub>2</sub> as a predominant N-glycan structure or a predominant intermediate N-glycan structure.

108. (Canceled)

109. (Currently amended) The method of claim [[108]]107, wherein said ER-retention signal comprises the peptide HDEL (SEQ ID NO: 1).

110. (Previously presented) The method of claim 107, wherein the nucleotide sequence coding for said  $\alpha$ -1,2-mannosidase or said functional part is operably linked to a promoter and a 3' termination sequence.

111. (Previously presented) The method of claim 109, wherein said promoter is the promoter of a gene selected from the group consisting of AOXI, AOXII, GAP, and FLD.

112. (Previously presented) The method of claim 107, wherein the strain is a *Pichia pastoris* strain.

113. (Canceled)

114. (New) The strain of claim 90, wherein the Och1 disruption is the sole genetic disruption of the Golgi mannosyl transferases acting in N-glycosylation of said strain.

115. (New) The method of claim 107, wherein the Och1 disruption is the sole genetic disruption of the Golgi mannosyl transferases acting in N-glycosylation of said strain.